that the microsomal enzyme, steroid sulfatase, is deficient in all patients with recessive X-linked ichthyosis.

Diagnosis of this disorder may be established by several methods. Prenatally, it can be inferred from a characteristic profile of maternal estrogen excretion and confirmed through direct enzyme assay in cultured fetal amniocytes. Postnatally, steroid sulfatase activity can be assayed in cultured fibroblasts or fresh leukocytes. The diagnosis can also be inferred from the accumulation of cholesterol sulfate, a substrate of the enzyme, in scale from these patients and in serum and erythrocyte membranes. In serum, cholesterol sulfate is carried on predominantly low-density lipoproteins (LDL); in cases of recessive X-linked ichthyosis, accumulation of cholesterol sulfate in LDL results in increased electronegativity of these particles—hence their altered electrophoretic mobility on lipoprotein electrophoresis. Thus, a readily available standard laboratory test may be used for the diagnosis of this disorder.

Other forms of ichthyosis have also been linked to abnormalities in epidermal lipid metabolism. This association is not surprising in view of the structure of stratum corneum, in which anucleated, keratinized corneocytes are surrounded by an extracellular matrix composed of neutral lipids (especially alkanes, triglycerides, free fatty acids, cholesterol and ceramides). Alterations in the composition of the extracellular lipid matrix affect the normal process of desquamation. Cholesterol sulfate, a highly amphipathic lipid, is one of the few remaining polar lipids in stratum corneum. Its hydrolytic enzyme, steroid sulfatase, also localizes to the intercellular regions of stratum corneum. Continuing hydrolysis of cholesterol sulfate as corneocytes move outward may be a critical factor leading to normal desquamation. In the stratum corneum of patients with recessive X-linked ichthyosis, absence of steroid sulfatase activity results in continued high levels of cholesterol sulfate, reduced levels of free sterol and impaired desquamation.

MARY L. WILLIAMS, MD
San Francisco

REFERENCES

Elias PM, Williams ML, Maloney ME, et al: Stratum corneum lipids in disorders of cornification—Steroid sulfatase and cholesterol sulfate in normal desquamation and the pathogenesis of recessive X-linked ichthyosis. J Clin Invest 1984 Oct; 74:1414-1421

Epstein EH Jr, Krauss RM, Shackleton CH: X-linked ichthyosis: Increased blood cholesterol sulfate and electrophoretic mobility of low-density lipoprotein. Science 1981 Nov 6; 214:659-660

Williams ML: The ichthyoses—Pathogenesis and prenatal diagnosis: A review of recent advances. Pediatr Dermatol 1983 Jul; 1:1-24

Subsets of Systemic Lupus Erythematosus

NEWLY DEFINED SUBSETS of lupus erythematosus are of value in defining prognosis and suggesting management approaches.

Subacute cutaneous lupus erythematosus is a cutaneous lupus variant characterized by mild systemic disease and slow therapeutic response. The lesions may be annular and polycyclic or papulosquamous and psoriasiform. Areas involved usually are the shoulders, upper chest and back. There is little scarring, photosensitivity is common and patients usually have mild systemic disease. Serologic markers of subacute cutaneous lupus include HLA-DR3 and the antibody anti-Ro (SSA [Sjögren's syndrome antibody]). In patients whose diagnosis is a problem, skin biopsy for hematoxylin-eosin stain and immunopathology should be done. In addition to the usual lupus serologic tests, studies for anti-Ro (SSA) antibody and HLA-DR3 may help to define the problem. It is important to differentiate the psoriasiform type from psoriasis, as therapy for psoriasis—that is, ultraviolet light—is contraindicated in patients with lupus.

Neonatal lupus erythematosus is a subset in which patients may or may not have cutaneous lesions. A "raccoon rash" is most common, though discoid and subacute cutaneous lupus lesions also occur. Mothers of these children may have clinical or serologic features of connective tissue disease. Systemic features of neonatal lupus include congenital heart block, hepatosplenomegaly and failure to thrive. Antinuclear antibodies are usually found, and the anti-Ro (SSA) antibody seems to be a marker in the patients and their mothers. The anti-Ro (SSA) antibody may be useful in prenatal screening of mothers with connective tissue disease and in identifying neonates at high risk for the development of congenital heart block.

DENNY L. TUFFANELLI, MD
San Francisco

REFERENCES

McCue CM, Mantakas ME, Tingelstad JB, et al: Congenital heart block in newborns of mothers with connective tissue disease. Circulation 1977 Jul; 56:82-90

Sontheimer RD, Maddison PJ, Reichlin M, et al: Serologic and HLA associations in subacute cutaneous lupus erythematosus, a clinical subset of lupus erythematosus. Ann Intern Med 1982 Nov; 97:664-671

Sontheimer RD, Thomas JR, Gilliam JN: Subacute cutaneous lupus erythematosus: A cutaneous marker for a distinct lupus erythematosus subset. Arch Dermatol 1979 Dec; 115:1409-1415

Leukotrienes—Their Importance in Dermatology

THE LEUKOTRIENES CONSTITUTE a group of derivatives of arachidonic acid that were so named because they were first isolated from preparations of leukocytes and were all found to possess three conjugated double bonds. Neutrophils, macrophages, eosinophils, basophils and some populations of mast cells are capable of generating leukotrienes. Leukotrienes C_4, D_4 and E_4 (abbreviated LTC_4, LTD_4 and LTE_4) are unique among the known metabolites of arachidonic acid—which include the prostaglandins and thromboxanes—in respectively having the tripeptide glutathione, the dipeptide cysteinyl-glycine and cysteine alone, linked to the arachidonic acid skeleton. LTC_4 and LTD_4 constitute the major part of the activity that was previously called slow-reacting substance of anaphylaxis. In the skin, these two compounds cause increased permeability of postcapillary venules. Most significant, LTC_4 and LTD_4 are at least 1,000-fold more potent on a molar basis than is histamine. When injected into human skin, LTC_4 and LTD_4 produce classic urticaria, suggesting that these agents may be involved in the production of some types of urticaria, especially those that are unresponsive to antihistamine therapy. Unlike the prostaglandins and thromboxanes, the generation of leukotrienes is not suppressed by most nonsteroidal anti-inflammatory drugs such as aspirin, indomethacin or ibuprofen. However, corticosteroids do inhibit the generation of leukotrienes as well as the prostaglandins and thromboxanes.

Another leukotriene, designated LTB_4, which does not